PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 1 **January 1992**

CONTENTS

REVIEW

Drug Metabolism in the Nasal Mucosa 1
Mohamadi A. Sarkar

RESEARCH ARTICLES

Composite Poly(vinyl alcohol) Beads for Controlled Drug Delivery *(PDD)* 10
Cherng-Ju Kim and Ping I. Lee

Estimation of Permanence Time, Exit Time, Dilution Factor, and Steady-State Volume of Distribution *(PPDM)* 17
Joyce Mordenti and Aldo Rescigno

The Influence of Polymer Glass Transition Temperature and Molecular Weight on Drug Release from Tablets Containing Poly(DL-lactic Acid) *(PT)* 26
Marcelo O. Omelczuk and James W. McGinity

REPORTS

Lyophilized Formulations of Recombinant Tumor Necrosis Factor *(Biotec)* 33
Maninder S. Hora, Rajsharan K. Rana, and Flint W. Smith

Controlled Protein Release from Polyethyleneimine-Coated Poly(L-lactic Acid)/Pluronic Blend Matrices *(Biotec/PDD)* 37
Tae Gwan Park, Smadar Cohen, and Robert Langer

Localization of Epidermal Growth Factor (EGF) Binding Sites on Antiluminal Plasma Membrane of Rat Kidney: Autoradiographic Study Using Nonfiltering Perfused Rat Kidney *(Pharmacol/PPDM)* 40
Dong Chool Kim, Yuichi Sugiyama, Yasushi Kanai, Norio Ohnuma, and Manabu Hanano

Feasibility of Measuring the Bioavailability of Topical Betamethasone Dipropionate in Commerical Formulations Using Drug Content in Skin and a Skin Blanching Bioassay *(PDD)* 45
Lynn K. Pershing, Barbara S. Silver, Gerald G. Krueger, Vinod P. Shah, and Jerome P. Skelley

Tolerability and Absorption Enhancement of Intranasally Administered Octreotide by Sodium Taurodihydrofusidate in Healthy Subjects *(PDD)* 52
Thomas Kissel, Juergen Drewe, Siegfried Bantle, Andreas Rummelt, and Christoph Beglinger

Dissolution of Ionizable Drugs into Unbuffered Solution: A Comprehensive Model for Mass Transport and Reaction in the Rotating Disk Geometry *(PDD)* 58
Marylee Z. Southard, Don W. Green, Valentino J. Stella, and Kenneth J. Himmelstein

A Surface Energy Analysis of Mucoadhesion: Contact Angle Measurements on Polycarbophil and Pig Intestinal Mucosa in Physiologically Relevant Fluids *(PDD)* 70
Claus-Michael Lehr, Joke A. Bouwstra, Harry E. Boddé, and Hans E. Junginger

Buffer Effects on Swelling Kinetics in Polybasic Gels *(PDD)* 76
Ronald A. Siegel, Ingegerd Johannes, C. Anthony Hunt, and Bruce A. Firestone

Influence of Formulation, Receptor Fluid, and Occlusion on *in Vitro* Drug Release from Topical Dosage Forms, Using an Automated Flow-Through Diffusion Cell *(PDD)* 82
Alain Rolland, Gilles Demichelis, Jean-Claude Jamoulle, and Braham Shroot

Self-Emulsifying Drug Delivery Systems: Formulation and Biopharmaceutic Evaluation of an Investigational Lipophilic Compound *(PDD)* 87
Susan A. Charman, William N. Charman, Mark C. Rogge, Terry D. Wilson, Frank J. Dutko, and Colin W. Pouton

Complexation Studies of Cyclodextrins with Tricyclic Antidepressants Using Ion Selective Electrodes *(PDD/APQ)* 94
Georgia N. Valsami, Michael A. Koupparis, and Panayotis E. Macheras

CONTENTS (Continued)

A Sensitive and Specific Procedure for Quantitation of ADR-529 in Biological Fluids by High-Performance Liquid Chromatography (HPLC) with Column Switching and Amperometric Detection *(APQ)* 101
Richard C. Lewis, Barbara A. Phillips, John R. Baldwin, David T. Rossi, and Prem K. Narang

Evaluation of the Physical Stability of Freeze-Dried Sucrose-Containing Formulations by Differential Scanning Calorimetry *(APQ)* 109
Marcel P. W. M. te Booy, Rien A. de Ruiter, and André L. J. de Meere

Analysis of Hydroxyurea in Capsules and Aqueous Solution and Stability Study with Capillary Gas Chromatography and Thermionic (N–P) Specific Detection *(APQ)* 115
Adnan El-Yazigi and Sameer Al-Rawithi

Validation of a Column-Switching High-Performance Liquid Chromatographic (HPLC) Method for Determination of ML-1035 and Its Five Metabolites in Plasma *(APQ)* 119
Be-Sheng Kuo, James C. Poole, and Kin-Kai Hwang

Surface Characterization of Activated Charcoal by X-Ray Photoelectron Spectroscopy (XPS): Correlation with Phenobarbital Adsorption Data *(APQ)* 126
Gerald M. Burke, Dale Eric Wurster, Mary J. Berg, Peter Veng-Pedersen, and Dorothy D. Schottelius

Kinetics of Degradation of Levothyroxine in Aqueous Solution and in Solid State *(APQ)* 131
Chong Min Won

Kinetic Study of the Transformation from Tetrahydrate to Monohydrate of a New Antiallergic, Sodium 5-(4-oxo-phenoxy-4H-quinolizine-3-carboxamide)-tetrazolate *(APQ/MNPC)* 138
Satoshi Kitamura, Toshiji Tada, Yoshihiko Okamoto, and Tsutomu Yasuda

Bisacylphosphonates Inhibit Hydroxyapatite Formation and Dissolution *in Vitro* and Dystrophic Calcification *in Vivo* *(MNPC/Pharmacol)* 143
Gershon Golomb, Ada Schlossman, Hanan Saadeh, Matilda Levi, Joel M. Van Gelder, and Eli Breuer

Poly(L-lactic Acid) Microspheres Containing Neutron-Activatable Holmium-165: A Study of the Physical Characteristics of Microspheres Before and After Irradiation in a Nuclear Reactor *(PT/PDD)* 149
Russell J. Mumper and Michael Jay

TECHNICAL NOTE
Potential Use of Microdialysis in Pharmacokinetics: A Protein Binding Study *(PPDM)* 155
Marianne Ekblom, Margareta Hammarlund-Udenaes, Thomas Lundqvist, and Per Sjöberg

LETTER TO THE EDITOR 159

EDITORIAL 160

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 2 **February 1992**

CONTENTS

RESEARCH ARTICLES

Pharmacokinetic Analysis of Drug Absorption from Muscle Based on a Physiological Diffusion Model: Effect of Molecular Size on Absorption *(PDD/PPDM)* 161
Eiji Nara, Masaaki Masegi, Tetsuya Hatono, and Mitsuru Hashida

An Experimental Design Strategy for Quantitating Complex Pharmacokinetic Models: Enterohepatic Circulation with Time-Varying Gallbladder Emptying as an Example *(PPDM)* 169
Yow-Ming Chen Wang and Richard H. Reuning

REPORTS

Potentiation of Cytotoxicity of Mitoxantrone Toward CHO-K1 Cells *in Vitro* by Dipyridamole *(Pharmacol)* 178
Pankaj B. Desai and Rajagopalan Sridhar

A Novel Approach for the Determination of the Pain-Producing Potential of Intravenously Injected Substances in the Conscious Rat *(Pharmacol)* 182
John W. Marcek, William J. Seaman, and Royal J. Weaver

Cutaneous Metabolism of Nitroglycerin *in Vitro*. I. Homogenized Versus Intact Skin *(PPD)* 187
Naruhito Higo, Robert S. Hinz, David T.W. Lau, Leslie Z. Benet, and Richard H. Guy

Enhanced Bioavailability of Cefoxitin Using Palmitoyl L-Carnitine. I. Enhancer Activity in Different Intestinal Regions *(PDD)* 191
Steven C. Sutton, Edward L. LeCluyse, Leilani Cammack, and Joseph A. Fix

Hydrophobic Anionic Gel Beads for Swelling-Controlled Drug Delivery *(PDD)* 195
Cherng-Ju Kim and Ping I. Lee

Biodegradable Pseudolatexes: The Chemical Stability of Poly(D,L-Lactide) and Poly(ε-Caprolactone) Nanoparticles in Aqueous Media *(PDD)* 200
Mark D. Coffin and James W. McGinity

Development of Extended-Release Solid Dispersions of Nonsteroidal Antiinflammatory Drugs with Aqueous Polymeric Dispersions: Optimization of Drug Release via a Curve-Fitting Technique *(PDD)* 206
Chris Ho and George Chiaw-Chi Hwang

Determination of Lidocaine Concentrations in Skin After Transdermal Iontophoresis: Effects of Vasoactive Drugs *(PDD)* 211
J. Edmond Riviere, Nancy A. Monteiro-Riviere, and Alfred O. Inman

An Electrically Modulated Drug Delivery Device. II. Effect of Ionic Strength, Drug Concentration, and Temperature *(PDD)* 215
Antony D'Emanuele and John N. Staniforth

Factors Affecting the Release Rate of Terbutaline from Liposome Formulations After Intratracheal Instillation in the Guinea Pig *(PDD/PPDM)* 220
Robert M. Fielding and Robert M. Abra

CONTENTS (Continued)

Pharmacokinetic Evaluation of Drug Interactions with Anti-Human Immunotrophic Virus (HIV) Drugs. III. 2',3'-Dideoxycytidine (ddC) and Zidovudine in Monkeys *(PPDM)* 224
Mingxin Qian, Anne R. Swagler, Mehul Mehta, C.T. Vishwanathan, and James M. Gallo

Competitive Inhibition of Zidovudine Clearance by Probenecid During Continuous Coadministration *(PPDM)* 228
Shekman L. Wong, Mohsen A. Hedaya, and Ronald J. Sawchuk

Effect of Chronic Hypertension on the Blood–Brain Barrier Permeability of Libenzapril *(PPDM)* 236
Jian-ping Tang, Ashok Rakhit, Frank L. Douglas, and Srikumaran Melethil

Bioavailability of Leuprolide Acetate Following Nasal and Inhalation Delivery to Rats and Healthy Humans *(PPDM)* 244
Akwete Adjei, Dean Sundberg, James Miller, and Alexander Chun

Pharmaceutical Properties of Loracarbef: The Remarkable Solution Stability of an Oral 1-Carba-1-dethiacephalosporin Antibiotic *(APQ)* 250
Carol E. Pasini and Joseph M. Indelicato

Development and Evaluation of a Novel Dissolution Apparatus for Medicated Chewing Gum Products *(PT)* 255
James N. Rider, Ed L. Brunson, Walter G. Chambliss, Robert W. Cleary, Ahmed H. Hikal, Peggy H. Rider, Larry A. Walker, Christy M. Wyandt, and Alan B. Jones

Prolonged Systemic Delivery of Peptide Drugs by Long-Circulating Liposomes: Illustration with Vasopressin in the Brattleboro Rat *(Biotec/PDD)* 260
Martin C. Woodle, Gert Storm, Mary S. Newman, Jill J. Jekot, Lila R. Collins, Francis J. Martin, and Francis C. Szoka, Jr.

The Influence of Sucrose, Dextran, and Hydroxypropyl-β-cyclodextrin as Lyoprotectants for a Freeze-Dried Mouse IgG_{2a} Monoclonal Antibody (MN12) *(Biotec)* 266
Maaike E. Ressing, Wim Jiskoot, Herre Talsma, Cor W. van Ingen, E. Coen Beuvery, and Daan J.A. Crommelin

Renal Tubular Handling of *p*-Aminohippurate and Epidermal Growth Factor (EGF) in Filtering and Nonfiltering Perfused Rat Kidneys *(Biotec)* 271
Dong-Chool Kim, Yuichi Sugiyama, Yasufumi Sawada, and Manabu Hanano

TECHNICAL NOTE

Colonic Drug Delivery: Enhanced Release of Indomethacin from Cross-Linked Chondroitin Matrix in Rat Cecal Content *(PDD)* 276
Abraham Rubinstein, David Nakar, and Amnon Sintov

EUROPEAN REVIEWERS FOR PHARMACEUTICAL RESEARCH (November 1990–November 1991) 279

ASSOCIATION NEWS AND ANNOUNCEMENTS 281

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 3 **March 1992**

CONTENTS

REVIEW

Hydrogels: Swelling, Drug Loading, and Release 283
Sung Wan Kim, You Han Bae, and Teruo Okano

RESEARCH ARTICLE

Pharmacokinetic/Dynamic Correlation of Pulmonary and Cardiac Effects of Fenoterol in Asthmatic Patients After Different Routes of Administration *(PPDM)* 291
Günther Hochhaus, Ernst-Wilhelm Schmidt, Karl L. Rominger, and Helmut Möllmann

REPORTS

The Bilayer Floating Capsule: A Stomach-Directed Drug Delivery System for Misoprostol *(PDD)* 298
Marianne Oth, Michel Franz, Jacques Timmermans, and Andre Moës

Cutaneous Metabolism of Nitroglycerin *in Vitro*. II. Effects of Skin Condition and Penetration Enhancement *(PDD)* 303
Naruhito Higo, Robert S. Hinz, David T. W. Lau, Leslie Z. Benet, and Richard H. Guy

Rotating-Disk Dissolution Kinetics of Nitrofurantoin Anhydrate and Monohydrate at Various Temperatures *(PDD)* 307
Makoto Otsuka, Reiko Teraoka, and Yoshihisa Matsuda

An Electrically Modulated Drug Delivery Device. III. Factors Affecting Drug Stability During Electrophoresis *(PDD)* 312
Antony D'Emanuele and John N. Staniforth

Simultaneous *in Vitro* Measurement of Intestinal Tissue Permeability and Transepithelial Electrical Resistance (TEER) Using Sweetana–Grass Diffusion Cells *(PDD)* 316
Steven C. Sutton, Alexander E. Forbes, Robyn Cargill, Jerome H. Hochman, and Edward L. LeCluyse

Intestinal Absorption of Peptides and Peptide Analogues: Implications of Fasting Pancreatic Serine Protease Levels and pH on the Extent of Oral Absorption in Dogs and Humans *(PDD/Biotec)* 320
Patrick J. Sinko

Mechanism and Site Dependency of Intestinal Mucosal Transport and Metabolism of Thymidine Analogues *(PDD/PPDM)* 326
Gee-Bae Park and Ashim K. Mitra

Analysis of Zidovudine Distribution to Specific Regions in Rabbit Brain Using Microdialysis *(PPDM)* 332
Shekman L. Wong, Yanfeng Wang, and Ronald J. Sawchuk

Uptake and Stereoselective Binding of the Enantiomers of MK-927, a Potent Carbonic Anhydrase Inhibitor, by Human Erythrocytes *in Vitro* *(PPDM)* 339
Jiunn H. Lin, Tsu-Han Lin, and Haiyung Cheng

Population Characteristics of Biological Systems Influenced by Multicomponent Random and Uniform Variation *(PPDM)* 345
Gregory M. Kochak

Use of a Pharmacokinetic Model Incorporating Discontinuous Gastrointestinal Absorption to Examine the Occurrence of Double Peaks in Oral Concentration–Time Profiles *(PPDM)* 350
A. Benjamin Suttle, Gary M. Pollack, and Kim L. R. Brouwer

Bacterial Monitoring in Vials Using a Spectrophotometric Assimilation Method *(APQ)* 357
Leonard J. Galante, Michael A. Brinkley, and Robert A. Lodder

The Structure of Celiprolol *(MNPC)* 365
Narendra Kumar, Christianna Strohbeck, and Herman L. Ammon

New Water-Soluble Pilocarpine Derivatives with Enhanced and Sustained Muscarinic Activity *(MNPC)* 372
Pascal Druzgala, David Winwood, Malgorzata Drewniak-Deyrup, Scott Smith, Nicholas Bodor, and James J. Kaminski

The Anomalous Hydrolytic Behavior of 1-Phenylvinyl Phosphate *(MNPC)* 378
Albert S. Kearney and Valentino J. Stella

Evaluation of the Poisson Distribution for Estimating the Quality of Drug/Diluent Random Powder Mixtures. I. High Particle Size of the Drug Constituent *(PT)* 385
Herbert Egermann, Peter Frank, and Anna Krumphuber

Optimized Formulation of Magnetic Chitosan Microspheres Containing the Anticancer Agent, Oxantrazole *(PT)* 390
Emad Eldin Hassan, Roy C. Parish, and James M. Gallo

Mechanisms to Control Drug Release from Pellets Coated with a Silicone Elastomer Aqueous Dispersion *(PT)* 398
Terrence C. Dahl and I-Ian T. Sue

Effect of Surfactant Phase in Perfluorocarbon Emulsification Efficiency *(PT)* 406
Jean M. Pasternacki-Surian, Roger L. Schnaare, and Edwin T. Sugita

A Novel Method for Determination of Sterility of Microcapsules and Measurement of Viability of Encapsulated Organisms *(PT)* 410
K. Keith Kwok and Diane J. Burgess

Application of Curdlan to Controlled Drug Delivery. I. The Preparation and Evaluation of Theophylline-Containing Curdlan Tablets *(PT/PDD)* 414
Motoke Kanke, Keiko Koda, Yoko Koda, and Hirokazu Katayama

The Disposition of a Human Relaxin (hRlx-2) in Pregnant and Nonpregnant Rats *(Biotec/PPDM)* 419
Paul A. Cossum, Kevin A. Dwyer, Michael Roth, Sharon A. Chen, Barbara Moffat, Richard Vandlen, and Bobbe L. Ferraiolo

Sustained Delivery of Interleukin-2 from a Poloxamer 407 Gel Matrix Following Intraperitoneal Injection in Mice *(Biotec/PDD)* 425
Thomas P. Johnston, Monika A. Punjabi, and Christopher J. Froelich

The Influence of Peptide Structure on Transport Across Caco-2 Cells. II. Peptide Bond Modification Which Results in Improved Permeability *(Biotec/PDD)* 435
Robert A. Conradi, Allen R. Hilgers, Norman F. H. Ho, and Philip S. Burton

ASSOCIATION NEWS AND ANNOUNCEMENTS 440

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 4 **April 1992**

CONTENTS

RESEARCH ARTICLE

Polyalkylcyanoacrylate Nanoparticles as Polymeric Carriers for Antisense Oligonucleotides *(Biotec/PDD)* 441
Christine Chavany, Trung Le Doan, Patrick Couvreur, Francis Puisieux, and Claude Hélène

REPORTS

Correlation of *in Vitro* Release Rate and *in Vivo* Absorption Characteristics of Four Chlorpheniramine Maleate Extended-Release Formulations *(PPDM)* 450
Parviz Mojaverian, Elaine Radwanski, Chin-Chung Lin, Philip Cho, Winston A. Vadino, and Jack M. Rosen

Pharmacokinetic and Pharmacodynamic Comparison of Immediate-Release and Sustained-Release Adinazolam Mesylate Tablets After Single- and Multiple-Dose Administration *(PPDM)* 457
Joseph C. Fleishaker and C. Eugene Wright

The Pharmacokinetics of Trilostane and Ketotrilostane in an Interconverting System in the Rat *(PPDM)* 464
J. Paul McGee and P. Nicholas Shaw

Saturable Tissue Binding and Imirestat Pharmacokinetics in Rats *(PPDM)* 469
Jenny Y. Chien, Christopher R. Banfield, Romulus K. Brazzell, Philip R. Mayer, and John T. Slattery

Significance of Binding to Na,K-ATPase in the Tissue Distribution of Ouabain in Guinea Pigs *(PPDM)* 474
Hideyoshi Harashima, Michio Mamiya, Masayo Yamazaki, Yuichi Sugiyama, Yasufumi Sawada, Tatsuji Iga, and Manabu Hanano

The *in Situ* Acetylation of an Immobilized Human Serum Albumin Chiral Stationary Phase for High-Performance Liquid Chromatography in the Examination of Drug–Protein Binding Phenomena *(APQ)* 480
Terence A. G. Noctor and Irving W. Wainer

An Air-Gap Enzyme Electrode: Development and Applications *(APQ)* 485
Ravi M. Shanker, Nashed E. Nashed, and Siegfried Lindenbaum

Stereoselective Enzymatic Hydrolysis of Various Ester Prodrugs of Ibuprofen and Flurbiprofen in Human Plasma *(MNPC/PPDM)* 492
Niels Mørk and Hans Bundgaard

The *in Vitro* Enzymic Labilities of Chemically Distinct Phosphomonoester Prodrugs *(MNPC)* 497
Albert S. Kearny and Valentino J. Stella

Amino Acid Side-Chain Contributions to Free Energy of Transfer of Tripeptides from Water to Octanol *(MNPC)* 504
Aeri Kim and Francis C. Szoka Jr.

Nebulization of Liposomes. III. The Effects of Operating Conditions and Local Environment *(PT)* 515
Ralph W. Niven, Teresa M. Carvajal, and Hans Schreier

CONTENTS (Continued)

Infrared Imaging of Pharmaceutical Materials Undergoing Compaction *(PT)* 521
Simon R. Bechard and G. R. B. Down

Absorptive-Mediated Endocytosis of an Adrenocorticotropic Hormone (ACTH) Analogue, Ebiratide, into the Blood–Brain Barrier: Studies with Monolayers of Primary Cultured Bovine Brain Capillary Endothelial Cells *(Biotec/PDD)* 529
Tetsuya Terasaki, Susumu Takakuwa, Akira Saheki, Shuzo Moritani, Takesada Shimura, Shigeru Tabata, and Akira Tsuji

Aminopeptidase Activity in the Jejunal and Ileal Peyer's Patches of the Albino Rabbit *(Biotec/PDD)* 535
Eiji Hayakawa and Vincent H. L. Lee

Phagocytosis of Nanoparticles by Human Immunodeficiency Virus (HIV)-Infected Macrophages: A Possibility for Antiviral Drug Targeting *(PDD)* 541
Volker Schäfer, Hagen von Briesen, Reinhard Andreesen, Anne-Marie Steffan, Cathy Royer, Sabine Tröster, Jörg Kreuter, and Helga Rübsamen-Waigmann

Bioadhesion by Means of Specific Binding of Tomato Lectin *(PDD/Biotec)* 547
Claus-Michael Lehr, Joke A. Bouwstra, Wouter Kok, Arthur B. J. Noach, Albertus G. de Boer, and Hans E. Junginger

Influence of Supersaturation on the Pharmacodynamic Effect of Bupranolol After Dermal Administration Using Microemulsions as Vehicle *(PDD/PPDM)* 554
Jens Kemken, Albrecht Ziegler, and Bernd W. Müller

Sonophoresis. I. The Use of High-Frequency Ultrasound to Enhance Transdermal Drug Delivery *(PDD)* 559
D. Bommannan, Hirohisa Okuyama, Paul Stauffer, and Richard H. Guy

Characteristics of Association of Oleoyl Derivatives of 5-Fluorodeoxyuridine and Methotrexate with Low-Density Lipoproteins (LDL) *(PDD)* 565
P. Chris de Smidt and Theo J. C. van Berkel

Physicochemical Properties of the Novel Heteropolyanion Antiviral Hexapotassium-α-vanado-11-tungstoborate (DuP 925) *(PDD/APQ)* 570
Michael B. Maurin, Rodney D. Vickery, W. M. Bryant, III, and Munir A. Hussain

^{1}H-Nuclear Magnetic Resonance (NMR) Studies on the Inclusion Complex of Prostaglandin E_1 (PGE_1) with α-Cyclodextrin *(PDD)* 575
Bert Steffan, Wilfried Fischer, Günther Cordes, Ilona Habon, and Robert Müller

TECHNICAL NOTES

A Flexible Automated Dissolution Testing System for Use with Either USP Apparatus 1 or USP Apparatus 2 *(APQ)* 578
Jeanette D. Dunkle, Daniel J. Gleason, and Gerard C. Hokanson

Determination of Dissociation Constants of Selected Cyclodextrin–Benzaldehyde Inclusion Complexes Using Pulse Polarography *(APQ)* 582
Hee-Sook Choi, Ching-jer Chang, and Adelbert M. Knevel

BOOK REVIEWS

New Drugs for Asthma 585
Reviewed by Anthony J. Hickey

CONTENTS (Continued)

Skin Pharmacology and Toxicology—Recent Advances 585
Reviewed by Renuka H. Bhatt and Dennis P. West

Nitration, Methods and Mechanisms 586
Reviewed by Ludwig Bauer

Biomimetic Polymers 586
Reviewed by Ashim K. Mitra

CONFERENCE REPORT
Analytical Methods Validation: Bioavailability, Bioequivalence and Pharmacokinetic Studies 588
Vinod P. Shah, Kamal K. Midha, Shrikant Dighe, Iain J. McGilveray, Jerome P. Skelly, Avraham Yacobi, Thomas Layloff, C. T. Viswanathan, C. Edgar Cook, R. D. McDowall, Kenneth A. Pittman, and Sidney Spector

ASSOCIATION NEWS AND ANNOUNCEMENTS 593

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 5 **May 1992**

CONTENTS

REPORTS

Stability Studies of Gabapentin in Aqueous Solutions *(APQ)* 595
Elena Zour, Shahid A. Lodhi, Russell U. Nesbitt, Steven B. Silbering, and Pravin R. Chaturvedi

Analytical Method Comparison Based upon Statistical Power Calculations *(APQ)* 601
David J. Mazzo and Margaret Connolly

Effect of Water Mobility on Drug Hydrolysis Rates in Gelatin Gels *(APQ)* 607
Sumie Yoshioka, Yukio Aso, and Tadao Terao

Initial Studies on the *N*-Glucosylation of Phenobarbital by Mouse Liver Microsomes Using a Radiochemical High-Performance Liquid Chromatographic (HPLC) Method *(APQ/MNPC)* 613
William H. Soine, Hosai Safi, and Richard B. Westkaemper

Kinetics and Mechanism of Isomerization of Cyclosporin A *(APQ/MNPC)* 617
Reza Oliyai and Valentino J. Stella

Microbial Production of a Crisnatol Metabolite *(MNPC)* 623
Charles D. Hufford, Saleh H. El-Sharkawy, Tannis M. Jurgens, and Julie R. Mikell

A Phosphinic Acid Dipeptide Analogue to Stabilize Peptide Drugs During Their Intranasal Absorption *(MNPC/Biotec)* 626
Munir A. Hussain, Marguerita S. L. Lim, Krishnaswamy S. Raghavan, Nancy J. Rogers, Rommel Hidalgo, and Charles A. Kettner

Adsorption of Fluorescein Dyes on Albumin Microspheres *(PT/PDD)* 629
Kamel Egbaria and Michael Friedman

Prediction and Assessment of Flammability Hazards Associated with Metered-Dose Inhalers Containing Flammable Propellants *(PT)* 636
Richard N. Dalby

Analytical Control Procedures of Immunoreactivity for IgG and Fab Fragments Specific to Haptens *(Biotec/APQ)* 643
Nathalie J. Cano, Alain E. Sabouraud, Michel Urtizberea, Jean Carcagne, Michel Grandgeorge, and Jean Michel G. Scherrmann

Differences in the Enhancing Effects of Sodium Caprate on Colonic and Jejunal Drug Absorption *(PDD)* 648
Mikio Tomita, Toyohiro Sawada, Takahiro Ogawa, Hiroyuki Ouchi, Masahiro Hayashi, and Shoji Awazu

Gastrointestinal Transit and Systemic Absorption of Captopril from a Pulsed-Release Formulation *(PDD/PPDM)* 654
Ian R. Wilding, Stanley S. Davis, Massoud Bakhshaee, Howard N. E. Stevens, Robert A. Sparrow, and John Brennan

Heat-Induced Drug Release Rate and Maximal Targeting Index of Thermosensitive Liposome in Tumor-Bearing Mice *(PDD)* 658
Katsumi Iga, Yasuaki Ogawa, and Hajime Toguchi

CONTENTS (Continued)

Predicting Skin Permeability *(PDD)* 663
Russell O. Potts and Richard H. Guy

Equilibrium and Kinetic Factors Influencing Bile Sequestrant Efficacy *(PDD)* 670
Paul E. Luner and Gordon L. Amidon

Pharmacokinetic and Metabolic Disposition of *p*-Chloro-*m*-xylenol (PCMX) in Dogs *(PPDM)* 677
Angelica Dorantes and Salomon Stavchansky

Effect of an Acute Dose of Alcohol on the Pharmacokinetics of Oral Nifedipine in Humans *(PPDM)* 683
Saeed Qureshi, Sylvia Laganière, Gilles Caillé, Denys Gossard, Yves Lacasse, and Iain McGilveray

TECHNICAL NOTES

Esterase Activity Toward the Diastereomers of Cefuroxime Axetil in the Rat and Dog *(MNPC)* 687
Gerold L. Mosher, Julianne McBee, and David B. Shaw

Molecular Complexation: β-Cyclodextrin and Benzaldehyde Inclusion Complex *(MNPC/PDD)* 690
Hee-Sook Choi, Adelbert M. Knevel, and Chin-jer Chang

Pharmacokinetics of Droperidol in Healthy Volunteers Following Intravenous Infusion and Rectal Administration from an Osmotic Drug Delivery Module *(PPDM)* 694
Suneel K. Gupta, Mary Southam, and Stephen Hwang

Enhanced Bioavailability of 6-Mercaptopurine After Rectal Administration in Rats *(PPDM)* 697
Yasuhisa Kato, Takeji Matsushita, Tomomasa Yokoyama, and Kiminori Mohri

BOOK REVIEWS

Carotenoids: Chemistry and Biology 700
Reviewed by A. Douglas Kinghorn

Molecular and Cellular Biology of Multidrug Resistance in Tumor Cells 700
Reviewed by Alexander Neyfakh

ASSOCIATION NEWS AND ANNOUNCEMENTS 702

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 6 **June 1992**

CONTENTS

REVIEW

Anti-Aids Drug Development: Challenges and Strategies *(MNPC)* 703
Prem Mohan

RESEARCH ARTICLE

Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of Pharmaceutical Preparations *(Biotec/APQ)* 715
Jens Brange, Liselotte Langkjær, Svend Havelund, and Aage Vølund

REPORTS

Chemical Stability of Insulin. 2. Formation of Higher Molecular Weight Transformation Products During Storage of Pharmaceutical Preparations *(Biotec/APQ)* 727
Jens Brange, Svend Havelund, and Philip Hougaard

Derivatives of 4-(2-*N*,*N*-Di-*n*-propylaminoethyl)-5-hydroxyindole: Synthesis and Pharmacological Effects *(MNPC)* 735
Joseph G. Cannon, Ioannis Roufos, Sheng Xing Ma, and John Paul Long

Structural Modification Study of Anthracyclinones: Synthesis and Biological Activity of Several Derivatives of η-Pyrromycinone *(MNPC)* 739
Dun-Fu Liu, Hui Xiong, and Chia-Chung Cheng

Improved Delivery Through Biological Membranes. XLV. Synthesis, Physical-Chemical Evaluation, and Brain Uptake Studies of 2-Chloroethyl Nitrosourea Delivery Systems *(MNPC/PDD)* 743
Krishnaswamy Raghavan, Thorsteinn Loftsson, Marcus E. Brewster, and Nicholas Bodor

Parenteral Formulation of the Kappa Agonist Analgesic, DuP 747, via Micellar Solubilization *(PT)* 750
Munir A. Hussain, Lei-Shu Wu, Christopher Koval, and Arthur R. Hurwitz

Acceleration of Heat Transfer in Vial Freeze-Drying of Pharmaceuticals. II. A Fluid Cushion Device *(PT)* 753
Samuel H. Yalkowsky and Suresh D. Patel

Microencapsulation of Solid Dispersions: Release of Griseofulvin from Griseofulvin:Phospholipid Coprecipitates in Microspheres *(PT)* 759
Gopi K. Vudathala and James A. Rogers

The Pharmacokinetics of Pulmonary-Delivered Insulin: A Comparison of Intratracheal and Aerosol Administration to the Rabbit *(Biotec/PPDM)* 764
Paul Colthorpe, Stephen J. Farr, Glyn Taylor, Ian J. Smith, and David Wyatt

Conjunctival Penetration of Insulin and Peptide Drugs in the Albino Rabbit *(Biotec/PDD)* 769
Eiji Hayakawa, Du-Shieng Chien, Kazuhiro Inagaki, Akira Yamamoto, Wei Wang, and Vincent H. L. Lee

CONTENTS (Continued)

Immobilization of Active Urokinase on Albumin Microspheres: Use of a Chemical Dehydrant and Process Monitoring *(Biotec/PT)* 776
Kumaril Bhargava and Howard Y. Ando

Macrophage Activation by Polymeric Nanoparticles of Polyalkylcyanoacrylates: Activity Against Intracellular *Leishmania donovani* Associated with Hydrogen Peroxide Production *(Pharmacol/PPD)* 782
Rogério Gaspar, Véronique Préat, Fred R. Opperdoes, and Michel Roland

The Mobile Order Theory Versus UNIFAC and Regular Solution Theory-Derived Models for Predicting the Solubility of Solid Substances *(PDD/MNPC)* 788
Paul Ruelle, Michel Buchmann, Hô Nam-Tran, and Ulrich W. Kesselring

Cholesterol (Thermodynamic) Activity Determinations in Bile Salt–Lecithin–Cholesterol Systems and Cholesterol-Rich Liquid Crystalline Mesophase Formation *(PDD)* 792
Uday K. Jain, William I. Higuchi, Chen L. Liu, Paul H. Lee, and Norman A. Mazer

Plasma Concentration Clamping in the Rat Using a Computer-Controlled Infusion Pump *(PPDM)* 800
Lars L. Gustafsson, William F. Ebling, Eileen Osaki, Sandy Harapat, Donald R. Stanski, and Steven L. Shafer

Stability of the New Anticancer Platinum Analogue 1,2-Diaminomethyl-Cyclobutane-Platinum(II)-Lactate (Lobaplatin; D19466) in Intravenous Solutions *(APQ)* 808
Henk-Jan Guchelaar, Donald R. A. Uges, Paul Aulenbacher, Elisabeth G. E. de Vries, and Nanno H. Mulder

Simultaneous Microdetermination of Rifampin, Deacetylrifampin, Isoniazid, and Acetylisoniazid in Plasma by Liquid Chromatography with Dual Electrochemical and Spectrophotometric Detection *(APQ)* 812
Adnan El-Yazigi and Dale A. Raines

TECHNICAL NOTES

Comparison of Azone and Hexamethylene Lauramide in Toxicologic Effects and Penetration Enhancement of Cimetidine in Rabbit Eyes *(Toxicol/PDD)* 817
I. Maged Ismail, Chi-Chu Chen, Joseph B. Richman, Jon S. Andersen, and Diane D.-S. Tang Liu

Pharmacokinetics of Oral 2′,3′-Dideoxyinosine in Rats *(PPDM)* 822
M. Guillaume Wientjes and Jessie L.-S. Au

CONFERENCE REPORT

Opportunities for Integration of Pharmacokinetics, Pharmacodynamics, and Toxicokinetics in Rational Drug Development 826
Carl C. Peck, William H. Barr, Leslie Z. Benet, Jerry Collins, Robert E. Desjardins, Daniel E. Furst, John G. Harter, Gerhard Levy, Thomas Ludden, John H. Rodman, Lilly Sanathanan, Jerome J. Schentag, Vinod R. Shah, Lewis B. Sheiner, Jerome P. Skelly, Donald R. Stanski, Robert J. Temple, C. T. Viswanathan, Judi Weissinger, and Avraham Yacobi

ASSOCIATION NEWS AND ANNOUNCEMENTS 834

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 7 **July 1992**

CONTENTS

REVIEW

Biosensor Development 835
Jeffrey N. Roe

RESEARCH ARTICLE

Reversal of Signs of Induced Cotton Effects of Dicumarol-α_1-Acid Glycoprotein Systems by Phenothiazine Neuroleptics Through Ternary Complexation *(PPDM/MNPC)* 845
Toshimi Miyoshi, Ryuji Yamamichi, Toru Maruyama, and Masaki Otagiri

REPORTS

The Enantiomers of the Valproic Acid Analogue 2-*n*-Propyl-4-pentynoic Acid (4-yn-VPA): Asymmetric Synthesis and Highly Stereoselective Teratogenicity in Mice *(MNPC/Toxicol)* 850
Ralf-Siegbert Hauck and Heinz Nau

Microscopic Characterization of Particle Size and Shape: An Inexpensive and Versatile Method *(PT)* 856
Michael E. Houghton and Gregory E. Amidon

Sterile Filtration of a Parenteral Emulsion *(PT)* 860
Deborah M. Lidgate, Thomas Trattner, Richard M. Shultz, and Richard Maskiewicz

Dissociation of Insulin Oligomers by Bile Salt Micelles and Its Effect on α-Chymotrypsin-Mediated Proteolytic Degradation *(Biotec)* 864
Yuping Li, Zezhi Shao, and Ashim K. Mitra

Effect of Zinc Binding on the Structure and Stability of Fibrolase, a Fibrinolytic Protein from Snake Venom *(Biotec)* 870
Denise Pretzer, Brenda Schulteis, David G. Vander Velde, Christopher D. Smith, James W. Mitchell, and Mark C. Manning

Vaginal Absorption of Insulin in the Rat: Effect of Penetration Enhancers on Insulin Uptake and Mucosal Histology *(PDD)* 878
Julie L. Richardson, Lisbeth Illum, and Norman W. Thomas

The Influence of Different Strains and Age on *in Vitro* Rat Skin Permeability of Water and Mannitol *(PDD)* 884
Ian P. Dick and Robert C. Scott

Oral Delivery of a Renin Inhibitor Compound Using Emulsion Formulations *(PDD/Biotec)* 888
Tugrul T. Kararli, Thomas E. Needham, Marty Griffin, Grant Schoenhard, Leonard J. Ferro, and Lisa Alcorn

Intestinal Water and Solute Absorption Studies: Comparison of *in Situ* Perfusion with Chronic Isolated Loops in Rats *(PDD)* 894
Hsiao-Hwa Lu, James D. Thomas, Josef J. Tukker, and David Fleisher

Absorption of Flurbiprofen in the Fed and Fasted States *(PPDM)* 901
Jennifer B. Dressman, Rosemary R. Berardi, Grace H. Elta, Thomas M. Gray, Patricia A. Montgomery, Henry S. Lau, Katherine L. Pelekoudas, Gregory J. Szpunar, and John G. Wagner

Effect of Chronic Administration of Phenobarbital on the Hepatobiliary Transport of Phenol Red: Assessment by Statistical Moment Analysis *(PPDM)* 908
Toshiyuki Kakutani, Kaori Endo, Eiji Nara, Shigenobu Nakazora, and Mitsuru Hashida

Multiple Oral Administration of a Ketoprofen–Dextran Ester Prodrug in Pigs: Assessment of Gastrointestinal Bioavailability by Deconvolution *(PPDM)* 915
Frank Larsen, Bodil Hamborg Jensen, Henning Peter Olesen, and Claus Larsen

An *in Vitro* Pharmacodynamic Model to Simulate Antibiotic Behavior of Acute Otitis Media with Effusion *(PPDM)* 920
Kyle Vance-Bryan, Tom A. Larson, Mark W. Garrison, John P. Toscano, Daniel M. Canafax, and John C. Rotschafer

Bioequivalence *(PPDM)* 925
Aldo Rescigno

Method for the Determination of Diphenhydramine in Rabbit Whole Blood by High-Performance Liquid Chromatography (HPLC) with Ultraviolet (UV) Detection in Conjunction with Gas Chromatography (GC) with Mass Selective Detection (MSD) *(APQ)* 929
Karen M. Walters-Thompson and William D. Mason

Investigation of the Degradation Mechanisms of 5-Aminosalicylic Acid in Aqueous Solution *(APQ)* 933
Rita K. Palsmeier, Donna M. Radzik, and Craig E. Lunte

Solid-State Stability Testing of Drugs by Isothermal Calorimetry *(APQ)* 939
Michael J. Koenigbauer, Stephen H. Brooks, Gregory Rullo, and Richard A. Couch

TECHNICAL NOTES

Application of Electrospray Mass Spectrometry (ES-MS) for the Analysis of Monoclonal Antibody F_c Subunits *(Biotec/APQ)* 945
Wim Jiskoot, Gerrit Van de Werken, José M. Coco Martin, Brian N. Green, E. Coen Beuvery, and Daan J. A. Crommelin

Transdermal Delivery of Insulin to Alloxan-Diabetic Rabbits by Ultrasound Exposure *(PDD)* 952
Katsuro Tachibana

Electric Current-Sensitive Drug Delivery Systems Using Sodium Alginate/Polyacrylic Acid Composites *(PDD)* 955
Soon Hong Yuk, Sun Hang Cho, and Hai Bang Lee

Ideal Solubility of a Solid Solute: Effect of Heat Capacity Assumptions *(PDD)* 958
Dinesh S. Mishra and Samuel H. Yalkowsky

Physical Properties of Fast-Release Nonreverting Hydrochlorothiazide Solid Dispersions *(PDD)* 960
Mahasen M. Meshali and Khairy E. Gabr

Etorphine Is an Opiate Analgesic Physicochemically Suited to Transdermal Delivery *(PDD)* 963
Lynn M. Jolicoeur, M. Reza Nassiri, Charles Shipman Jr., Hoo-Kyun Choi, and Gordon L. Flynn

BOOK REVIEWS

NMR Methods for Elucidating Macromolecule-Ligand Interactions: An Approach to Drug Design 966
Reviewed by Michael E. Johnson

Biopharmaceutics and Clinical Pharmacokinetics 966
Reviewed by Keith A. Rodvold

ASSOCIATION NEWS AND ANNOUNCEMENTS 968

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 8 **August 1992**

CONTENTS

REVIEW

Structural Specificity of Mucosal-Cell Transport and Metabolism of Peptide Drugs: Implication for Oral Peptide Drug Delivery 969
Jane P. F. Bai and Gordon L. Amidon

RESEARCH ARTICLE

Novel Animal Model for Evaluating Topical Efficacy of Antiviral Agents: Flux Versus Efficacy Correlations in the Acyclovir Treatment of Cutaneous Herpes Simplex Virus Type 1 (HSV-1) Infections in Hairless Mice *(PDD)* 979
Paul H. Lee, Muh-Hwan Su, Earl R. Kern, and William I. Higuchi

REPORTS

Protein–Peptide Interactions as Probed by Tryptophan Fluorescence: Serum Albumins and Enkephalin Metabolites *(MNPC)* 990
Sunil Jain, C. Vijaya Kumar, and Devendra S. Kalonia

An Implantable Dosage Form for the Treatment of Bone Infections *(PT/PDD)* 993
Alekha K. Dash and Raj Suryanarayanan

Pharmacodynamics of Insulin Following Intravenous and Enteral Administrations of Porcine-Zinc Insulin to Rats *(Biotec/PPDM)* 1003
Robert J. Schilling and Ashim K. Mitra

Antisense c-*myc* Oligodeoxyribonucleotide Cellular Uptake *(Biotec/PDD)* 1010
Susanna Wu-Pong, Tania L. Weiss, and C. Anthony Hunt

Measurement of Serum [^{3}H]Tetracycline Kinetics and Indices of Kidney Function Facilitate Study of the Activity and Toxic Effects of Bisphosphonates in Bone Resorption *(Pharmacol)* 1018
Gershon Golomb, Yael Eitan, and Amnon Hoffman

Enhancement of Nasal Delivery of a Renin Inhibitor in the Rat Using Emulsion Formulations *(PDD/Biotec)* 1024
Tugrul T. Kararli, Thomas E. Needham, Grant Schoenhard, David A. Baron, R. Eric Schmidt, Barbara Katz, and Bayani Belonio

The Transport Barrier of Epithelia: A Comparative Study on Membrane Permeability and Charge Selectivity in the Rabbit *(PDD)* 1029
Yongyut Rojanasakul, Li-Ying Wang, Meenakshi Bhat, Douglas D. Glover, Carl J. Malanga, and Joseph K. H. Ma

Quantitative Evaluation of Aqueous Isopropanol Enhancement of Skin Flux of Terbutaline (Sulfate). I. Ion Associations and Species Equilibria in the Formulation *(PDD)* 1035
Punchun Liu, Tamie Kurihara-Bergstrom, Frank H. Clarke, Nina Gonnella, and William R. Good

Sonophoresis. II. Examination of the Mechanism(s) of Ultrasound-Enhanced Transdermal Drug Delivery *(PDD)* 1043
D. Bommannan, Gopinathan K. Menon, Hirohisa Okuyama, Peter M. Elias, and Richard H. Guy

CONTENTS (Continued)

Brain Parenchymal Metabolism of 5-Iodo-2-′-deoxyuridine and 5′-Ester Prodrugs *(PDD/PPDM)* 1048
Mridul K. Ghosh and Ashim K. Mitra

Disposition, Bioavailability and Serum Protein Binding of Pentachlorophenol in the B6C3F1 Mouse *(PPDM)* 1053
Bruno G. Reigner, Jean F. Rigod, and Thomas N. Tozer

Pharmacokinetic Analysis of the Structural Requirements for Forming "Stable" Analogues of Valpromide *(PPDM/MNPC)* 1058
Abdulla Haj-Yehia, Salim Hadad, and Meir Bialer

Pilocarpine Disposition and Salivary Flow Responses Following Intravenous Administration to Dogs *(PPDM)* 1064
Margaret L. Weaver, Jason M. Tanzer, and Paul A. Kramer

Nonlinear Disposition of Intravenous 2′,3′-Dideoxyinosine in Rats *(PPDM)* 1070
M. Guillaume Wientjes, Elora Mukherji, and Jessie L-S. Au

Is ICRF-187 [(+)-1,2-Bis(3,5-dioxopiperazinyl-1-yl)propane] Unusually Reactive for an Imide? *(APQ)* 1076
Jay M. Sisco and Valentino J. Stella

Formation of the Racemic Compound of Ephedrine Base from a Physical Mixture of Its Enantiomers in the Solid, Liquid, Solution, or Vapor State *(APQ)* 1083
Sarma P. Duddu and David J. W. Grant

Aqueous Stability and Solubility of CI-988, a Novel "Dipeptoid" Cholecystokinin-B Receptor Antagonist *(APQ)* 1092
Albert S. Kearney, Surendra C. Mehta, and Galen W. Radebaugh

TECHNICAL NOTES

Corticosteroid Pharmacodynamic Modeling: Osteocalcin Suppression by Prednisolone *(PPDM)* 1096
Jeffrey A. Wald and William J. Jusko

Inhibition of Hepatic and Cutaneous Biotransformation of Resorufin Ethers Following Intraperitoneal Administration of 1-Aminobenzotriazole *(PPDM/MNPC)* 1099
Neil F. Oldfield, Mildred Mortillo, William A. Garland, and Bruce A. Mico

Peptides Are Better Absorbed from the Lung than the Gut in the Rat *(Biotec/PDD)* 1103
Jennifer L. Hoover, Bob D. Rush, Karen F. Wilkinson, Jeff S. Day, Philip S. Burton, Thomas J. Vidmar, and Mary J. Ruwart

CONFERENCE REPORT

Principles and Criteria in the Development and Optimization of Topical Therapeutic Products 1107
Vinod P. Shah, Charan R. Behl, Gordon L. Flynn, William I. Higuchi, and Hans Schaefer

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 9 **September 1992**

CONTENTS

RESEARCH ARTICLE

Transport of Thyrotropin Releasing Hormone in Rabbit Buccal Mucosa *in Vitro* *(Biotec/PDD)* 1113
Martin E. Dowty, Kim E. Knuth, Brian K. Irons, and Joseph R. Robinson

REPORTS

Assessment of the Twin Impinger for Size Measurement of Metered-Dose Inhaler Sprays *(PT)* 1123
Nicholas C. Miller, Virgil A. Marple, Robert K. Schultz, and Wai Sing Poon

Calcium Alginate Beads as Core Carriers of 5-Aminosalicylic Acid *(PT)* 1128
Shun Y. Lin and James W. Ayres

Indomethacin-Loaded Microspheres: Design and Preparation by a Multiple-Emulsification Technique and Their *in Vitro* Evaluation *(PDD/PT)* 1132
Suranjana Roy, Manjusree Pal, and Bijan K. Gupta

Evaluation of Mucoadhesive Polymers in Ocular Drug Delivery. II. Polymer-Coated Vesicles *(PDD)* 1137
Nigel M. Davies, Stephen J. Farr, Jonathan Hadgraft, and Ian W. Kellaway

Percutaneous Absorption and Metabolism of Lonapalene in Psoriatic Skin *(PDD)* 1145
Paul A. Lehman, Raymond V. Tomlinson, Jerry I. Johnson, John E. Olerud, William A. Akers, and Thomas J. Franz

Correlation Between the Inhibitory Effects of Basic Drugs on the Uptake of Cardiac Glycosides and Taurocholate by Isolated Rat Hepatocytes *(PDD)* 1152
Kazuho Okudaira, Masayo Yamazaki, Yasufumi Sawada, Yuichi Sugiyama, Tatsuji Iga, and Manabu Hanano

Cyclodextrins as Nasal Absorption Promoters of Insulin: Mechanistic Evaluations *(PDD)* 1157
Zezhi Shao, Ramesh Krisnamoorthy, and Ashim K. Mitra

In Vivo Percutaneous Absorption of Hydrocortisone: Multiple-Application Dosing in Man *(PDD)* 1164
Joseph L. Melendres, Daniel A. W. Bucks, Etienne Camel, Ronald C. Wester, and Howard I. Maibach

Effects of Transdermal Penetration Enhancers on the Permeability of Shed Snakeskin *(PDD)* 1168
Tomoo Itoh, Lori Wasinger, T. Marjukka Turunen, and J. Howard Rytting

Enhanced Delivery of 5-Iodo-2′-Deoxyuridine to the Brain Parenchyma *(PDD/PPDM)* 1173
Mridul K. Ghosh and Ashim K. Mitra

Direct Suppression of Phagocytosis by Amphipathic Polymeric Surfactants *(PDD/Biotec)* 1177
Nancy Watrous-Peltier, Joann Uhl, Vivian Steel, Lynne Brophy, and Elaine Merisko-Liversidge

Nasal Membrane and Intracellular Protein and Enzyme Release by Bile Salts and Bile Salt–Fatty Acid Mixed Micelles: Correlation with Facilitated Drug Transport *(PDD)* 1184
Zezhi Shao and Ashim K. Mitra

Influence of Gastrointestinal Site of Drug Delivery on the Absorption Characteristics of Ranitidine *(PPDM)* 1190
Melissa F. Williams, George E. Dukes, William Heizer, Yieng-Hau Han, David J. Hermann, Thomas Lampkin, and Lawrence J. Hak

Molecular Weight-Dependent Lymphatic Transfer of Exogenous Macromolecules from Large Intestine of Renal Insufficiency Rats *(PPDM/Biotec)* 1195
Hiroshi Yoshikawa, Kanji Takada, and Shozo Muranishi

Quantitative Analysis of Mercaptoundecahydrododecaborate by Fourier Transform Infrared Spectroscopy *(APQ)* 1199
D. Robert Lu and Corey Munro

Solid-State Stability Studies of 13-*cis*-Retinoic Acid and All-*trans*-Retinoic Acid Using Microcalorimetry and HPLC Analysis *(APQ)* 1203
Xinyi Tan, Noel Meltzer, and Siegfried Lindenbaum

An Unexpected Hydrolysis pH–Rate Profile, at pH Values Less than 7, of the Labile Imide, ICRF-187: (+)-1,2-Bis-(3,5-dioxopiperazin-1-yl)propane *(MNPC)* 1209
Jay M. Sisco and Valentino J. Stella

TECHNICAL NOTES

A New Application Chamber for Skin Penetration Studies *in Vivo* with Liquid Preparations *(PT)* 1215
Claudia S. Leopold and Bernhard C. Lippold

Analysis of Pilocarpine and Its Degradation Products by Micellar Electrokinetic Capillary Chromatography *(APQ)* 1219
William N. Charman, Andrew J. Humberstone, and Susan A. Charman

Survey of Chlorinated Hydrocarbons and Other Organic Volatile Impurities in Captopril Raw Materials and Tablets *(APQ)* 1224
Terry D. Cyr, Robert C. Lawrence, and Edward G. Lovering

Determination of a Novel Calcium Channel Antagonist, Mepirodipine, in Plasma by Radioreceptor Assay Using (+)-[^{3}H]PN 200-110 *(APQ)* 1227
Shizuo Yamada, Youmei Matsuoka, Naoko Suzuki, Noriaki Sugimoto, Yoshihisa Kato, and Ryohei Kimura

BOOK REVIEWS

Reptile Venoms and Toxins 1231
Reviewed by Steven D. Aird

Pharmacy and the US Healthcare System 1231
Reviewed by J. Warren Salmon

LETTERS TO THE EDITOR 1233

OBITUARY 1234

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 10 **October 1992**

CONTENTS

RESEARCH ARTICLES

Delivery of Plasmid DNA into Mammalian Cell Lines Using pH-Sensitive Liposomes: Comparison with Cationic Liposomes *(Biotec)* 1235
Jean-Yves Legendre and Francis C. Szoka Jr.

Regional Jejunal Perfusion, A New *in Vivo* Approach to Study Oral Drug Absorption in Man *(PDD)* 1243
Hans Lennernäs, Örjan Ahrenstedt, Roger Hällgren, Lars Knutson, Märta Ryde, and Lennart K. Paalzow

REPORTS

Suppression of Inflammation by Cyclosporin A Is Mediated via a T-Lymphocyte-Independent Process *(Pharmacol)* 1252
Thomas E. Miller, Glenne Findon, and Douglas J. Ormrod

Microdialysis Sampling for the Investigation of Dermal Drug Transport *(PDD/APQ)* 1256
Joseph M. Ault, Craig E. Lunte, Noel M. Meltzer, and Christopher M. Riley

Acyclovir Permeation Enhancement Across Intestinal and Nasal Mucosae by Bile Salt–Acylcarnitine Mixed Micelles *(PDD)* 1262
Gee-Bae Park, Zezhi Shao, and Ashim K. Mitra

Effect of Loading on Swelling-Controlled Drug Release from Hydrophobic Polyelectrolyte Gel Beads *(PDD)* 1268
Cherng-Ju Kim and Ping I. Lee

Metabolism, Distribution, and Transdermal Permeation of a Soft Corticosteroid, Loteprednol Etabonate *(PDD)* 1275
Nicholas Bodor, Thorsteinn Loftsson, and Whei-mei Wu

Molecular Weight Changes in Polymer Erosion *(PDD)* 1279
Antony D'Emanuele, Jennifer Hill, Janet A. Tamada, Abraham J. Domb, and Robert Langer

Dose Proportionality of Transdermal Nitroglycerin *(PPDM)* 1284
R. C. Jewell, C. R. Banfield, D. A. Ruggirello, Y. W. Huang, P. K. Noonan, and M. A. Gonzalez

Metabolism of Testosterone During *in Vitro* Transport Across CACO-2 Cell Monolayers: Evidence for β-Hydroxysteroid Dehydrogenase Activity in Differentiated CACO-2 Cells *(PPDM/PDD)* 1290
Anders Buur and Niels Mørk

High-Dose Methotrexate Does Not Affect the Pharmacodynamics of Phenobarbital Hypnotic Action but Decreases the Central Nervous System (CNS) Sensitivity to Pentylenetetrazol-Induced Maximal Seizures in Rats *(PPDM)* 1295
Amnon Hoffman and Jose Alfon

Studies on the Excretion of Diazepam and Nordazepam into Milk for the Prediction of Milk-to-Plasma Drug Concentration Ratios *(PPDM)* 1299
Thomas Stebler and Theodor W. Guentert

CONTENTS (Continued)

General Treatment of the Enterohepatic Recirculation of Drugs and Its Influence on the Area Under the Plasma Level Curves, Bioavailability, and Clearance *(PPDM)* 1306
José-Esteban Peris-Ribera, Francisca Torres-Molina, M. Carmen Garcia-Carbonell, Juan Carlos Aristorena, and Luis Granero

Kinetics and Mechanism of Degradation of a Cyclic Hexapeptide (Somatostatin Analogue) in Aqueous Solution *(APQ)* 1314
Ramesh Krishnamoorthy and Ashim K. Mitra

A Quantitative Structure–Activity Relationship (QSAR) Study of Alkylpyrazine Odor Modalities *(MNPC)* 1321
Anna Tsantili-Kakoulidou and Lemont B. Kier

The Effects of *N*(4-Methylphenyl)diphenimide on Lipid Metabolism of Sprague Dawley Rats *(MNPC/Pharmacol)* 1324
Iris H. Hall, O. T. Wong, Rupendra Simlot, and David J. Reynolds

Microparticles of Polyvinyl Alcohol for Nasal Delivery. I: Generation by Spray-Drying and Spray-Desolvation *(PT)* 1330
Teck-Yeo Ting, Igor Gonda, and Elizabeth M. Gipps

Participation of Macrogolstearate 400 Lamellar Phases in Hydrophilic Creams and Vesicles *(PT)* 1336
Valentina Paspaleeva-Kühn and Eberhard Nürnberg

Benzoyl Peroxide Solubility and Stability in Hydric Solvents *(PT/APQ)* 1341
Eric M. Chellquist and William G. Gorman

Predicting the Effect of Nonionic Surfactants on Dispersed Droplet Radii in Submicron Oil-in-Water Emulsions *(PT)* 1347
Shawn Silvestri, Nandita Ganguly, and Esmail Tabibi

Powdered Solution Technology: Principles and Mechanism *(PT)* 1351
Spiros S. Spireas, Charles I. Jarowski, and Bhagwan D. Rohera

TECHNICAL NOTES

In Vitro Oral Mucosal Absorption of Liposomal Triamcinolone Acetonide *(PDD)* 1359
Stefan J. Sveinsson and Michael Mezei

Nasal Absorption of Leucine Enkephalin in Rats and the Effects of Aminopeptidase Inhibition, as Determined from the Percentage of the Dose Unabsorbed *(PDD)* 1362
Munir A. Hussain and Bruce J. Aungst

High-Performance Liquid Chromatography Determination of Acitretin in Plasma and Its Application to a Pharmacokinetic Study in Human Subjects *(APQ/PPDM)* 1365
Christian Surber, Jean-Philippe Laugier, Jean-Marie Geiger, Hot Bun, Alain Durand, and Howard I. Maibach

Inhibition of *myo*-Inositol 1-Phosphatase by *cis*-1,2,3-Cyclohexanetriol 1-Phosphate, a Molecular Simplification of the Natural Substrate *(MNPC)* 1370
Marc W. Harrold, Anong Sriburi, Paul Caimano, Hansheng Qi, David Seybert, and Fu-Tyan Lin

ASSOCIATION NEWS AND ANNOUNCEMENTS 1374

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 11 **November 1992**

CONTENTS

REVIEW

Monoclonal Antibodies in Hapten Immunoassays *(Biotec)* 1375
Olivier N. Chappey, Pierre Sandouk, and Jean-Michel G. Scherrmann

RESEARCH ARTICLES

An Alternative Approach for Assessment of Rate of Absorption in Bioequivalence Studies *(PPDM)* 1380
Mei-Ling Chen

Identification of Sites of Degradation in a Therapeutic Monoclonal Antibody by Peptide Mapping *(Biotec/APQ)* 1386
Daniel J. Kroon, Alysia Baldwin-Ferro, and Praful Lalan

REPORTS

Localization of Binding Sites for Epidermal Growth Factor (EGF) in Rat Kidney: Evidence for the Existence of Low Affinity EGF Binding Sites on the Brush Border Membrane *(Pharmacol/Biotec)* 1394
Dong-Chool Kim, Manabu Hanano, Yasushi Kanai, Norio Ohnuma, and Yuichi Sugiyama

Skin Alteration and Convective Solvent Flow Effects During Iontophoresis II. Monovalent Anion and Cation Transport Across Human Skin *(PDD)* 1402
Sandra M. Sims, William I. Higuchi, and V. Srinivasan

Noninvasive *in Vivo* Percutaneous Absorption Measurements Using X-Ray Fluorescence *(PDD/APQ)* 1410
J. David Robertson, Elizabeth Ferguson, Michael Jay, and Dennis J. Stalker

Lamellar Structures Formed by Stratum Corneum Lipids *in Vitro:* A Deuterium Nuclear Magnetic Resonance (NMR) Study *(PDD)* 1415
William Abraham and Donald T. Downing

Local Enhanced Topical Delivery (LETD) of Drugs: Does It Truly Exist? *(PDD)* 1422
Stephen C. McNeil, Russell O. Potts, and Michael L. Francoeur

Physicochemical Properties of Salts of *p*-Aminosalicylic Acid. I: Correlation of Crystal Structure and Hydrate Stability *(PDD)* 1428
Robert T. Forbes, Peter York, Victor Fawcett, and Leonard Shields

In Vivo Evaluation of Enteric-Coated Naproxen Tablets Using Gamma Scintigraphy *(PDD)* 1436
Ian R. Wilding, John G. Hardy, R. Andrew Sparrow, Stanley S. Davis, Paul B. Daly, and John R. English

Distribution and Elimination of the Glycosidase Inhibitors 1-Deoxymannojirimycin and *N*-Methyl-1-Deoxynojirimycin in the Rat *in Vivo* *(PPDM)* 1442
Esther D. Faber, Roelof Oosting, Jacques J. Neefjes, Hidde L. Ploegh, and Dirk K. F. Meijer

CONTENTS (Continued)

Pharmacokinetic Disposition of Multiple Dose Transdermal Nicotine in Healthy Adult Smokers *(PPDM)* 1451
Gregory M. Kochak, Jim X. Sun, R. Leslie Choi, and Anthony J. Piraino

Age and the Pharmacokinetic–Pharmacodynamic Relationship of Phenobarbital in Rats: "Pseudo"-Longitudinal vs Cross-Sectional Study Design *(PPDM)* 1456
Annemiek M. Stijnen, Meindert Danhof, and Cornelius F. A. van Bezooijen

Glutathione *S*-Transferase-Mediated Metabolism of Glyceryl Trinitrate in Subcellular Fractions of Bovine Coronary Arteries *(PPDM)* 1460
David T.-W. Lau, Elaine K. Chan, and Leslie Z. Benet

Kinetics and Mechanism of Degradation of Zileuton, a Potent 5-Lipoxygenase Inhibitor *(APQ)* 1465
Francisco J. Alvarez and Russell T. Slade

Synthesis of 2-(3-Substituted-1,2,4-oxadiazol-5-yl)-8-methyl-8-azabicyclo[3.2.1]octanes and 2α-(3-Substituted-1,2,4-oxadiazol-5-yl)-8-methyl-8-azabicyclo[3.2.1]oct-2-enes as Potential Muscarinic Agonists *(MNPC)* 1474
David J. Triggle, Yong Wha Kwon, Philip Abraham, M. Abdur Rahman, and F. Ivy Carroll

Relative Lipophilicities and Structural–Pharmacological Considerations of Various Angiotensin-Converting Enzyme (ACE) Inhibitors *(MNPC)* 1480
Sunanda A. Ranadive, Andrew X. Chen, and Abu T. M. Serajuddin

The Development of a Microwave Fluid-Bed Processor. I. Construction and Qualification of a Prototype Laboratory Unit *(PT)* 1487
Michael K. Doelling, David M. Jones, Richard A. Smith, and Robert A. Nash

The Development of a Microwave Fluid-Bed Processor. II. Drying Performance and Physical Characteristics of Typical Pharmaceutical Granulations *(PT)* 1493
Michael K. Doelling and Robert A. Nash

TECHNICAL NOTES

In Vivo Evaluation of Biodegradable Progesterone Microspheres in Mares *(PDD/PPDM)* 1502
Pramod K. Gupta, Rahul C. Mehta, Robert H. Douglas, and Patrick P. DeLuca

Sustained Propranol Delivery and Increased Oral Bioavailability in Dogs Given a Propranolol Laurate Salt *(PDD)* 1507
Bruce J. Aungst and Munir A. Hussain

Relationship Between Polymer Viscosity and Drug Release from a Matrix System *(PDD)* 1510
Lucy Wan Sai Cheong, Paul Wan Sia Heng, and Lee Fun Wong

Effect of Isoflurane Anesthesia on Antipyrine Pharmacokinetics in the Rat *(PPDM)* 1515
Francis L. S. Tse, David F. Nickerson, and Renee Aun

Employing Ionization Behaviors to Resolve a Trace-Level Impurity: Determination of 1,4-Dihydro-2,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridinedicarboxylic Acid Di-2-[methyl(phenylmethyl)amino]ethyl Ester in Nicardipine Drug Substance *(APQ)* 1518
Michael B. Maurin, Rodney D. Vickery, Philip Ma, Joseph Manalo, and Munir A. Hussain

Degradation of Synthetic Salmon Calcitonin in Aqueous Solution *(Biotec)* 1521
Kang Choon Lee, Yoon Joong Lee, Hyun Myo Song, Chang Ju Chun, and Patrick P. DeLuca

ASSOCIATION NEWS AND ANNOUNCEMENTS 1524

PHARMACEUTICAL RESEARCH

Official Journal of the American Association of Pharmaceutical Scientists

Volume 9 Number 12 **December 1992**

CONTENTS

RESEARCH ARTICLE

Instrumentation of a High-Shear Mixer: Evaluation and Comparison of a New Capacitive Sensor, a Watt Meter, and a Strain-Gage Torque Sensor for Wet Granulation Monitoring *(PT)* 1525
Vincent Corvari, William C. Fry, William L. Seibert, and Larry Augsburger

REPORTS

Lymphatic Targeting of Polymeric Nanoparticles After Intraperitoneal Administration in Rats *(PDD)* 1534
Philippe Maincent, Pierre Thouvenot, Claude Amicabile, Maurice Hoffman, Jörg Kreuter, Patrick Couvreur, and Jean Philippe Devissaguet

Hydrogels for Site-Specific Drug Delivery to the Colon: *In Vitro* and *in Vivo* Degradation *(PDD)* 1540
Helle Brøndsted and Jindřich Kopeček

The Influence of Liquid Crystalline Phases on Drug Percutaneous Absorption. I. Development of a Vehicle *(PDD)* 1546
James Swarbrick and James R. Siverly

The Influence of Liquid Crystalline Phases on Drug Percutaneous Absorption. II. Permeation Studies Through Excised Human Skin *(PDD)* 1550
James Swarbrick and James R. Siverly

Mixed Micelles as Proliposomes for the Solubilization of Teniposide *(PDD)* 1556
Hayat Alkan-Onyuksel and Kyonghee Son

Mucoadhesion of Copolymers and Mixtures Containing Polyacrylic Acid *(PDD)* 1563
Florence Thermes, Jeffrey Grove, Annouk Rozier, Bernard Plazonnet, Alain Constancis, Claude Bunel, and Jean-Pierre Vairon

Determination of Association Constants in Cyclodextrin/Drug Complexation Using the Scatchard Plot: Application to β-Cyclodextrin-Anilinonaphthalenesulfonates 1568
Evangelos E. Sideris, Georgia N. Valsami, Michael A. Koupparis, and Panayotis E. Macheras

Percutaneous Absorption Enhancement of Leuprolide *(PDD)* 1575
Mou-ying Fu Lu, Dennis Lee, and G. Subba Rao

Permeability Characteristics of Various Intestinal Regions of Rabbit, Dog, and Monkey *(PDD)* 1580
Nancy Jezyk, Werner Rubas, and George M. Grass

Influence of Permanent Cannulation of the Jugular Vein on Pharmacokinetics of Amoxycillin and Antipyrine in the Rat *(PPDM)* 1587
Francisca Torres-Molina, Juan-Carlos Aristorena, Carmen Garcia-Carbonell, Luis Granero, Jesús Chesa-Jiménez, José Pla-Delfina, and José-Esteban Peris-Ribera

Validation of Different Microdialysis Methods for the Determination of Unbound Steady-State Concentrations of Theophylline in Blood and Brain Tissue *(PPDM)* 1592
Per Sjöberg, Ing-Marie Olofsson, and Thomas Lundqvist

CONTENTS (Continued)

Decreased Systemic Clearance of Diltiazem with Increased Hepatic Metabolism in Rats with Uranyl Nitrate-Induced Acute Renal Failure *(PPDM)* 1599
Yong-Hee Lee, Min-Hwa Lee, and Chang-Koo Shim

Kinetic Modeling of Ouabain Tissue Distribution Based on Slow and Saturable Binding to Na,K-ATPase *(PPDM)* 1607
Hideyoshi Harashima, Michio Mamiya, Masayo Yamazaki, Yasufumi Sawada, Tatsuji Iga, Manabu Hanano, and Yuichi Sugiyama

The Bioinequivalence of Carbamazepine Tablets with a History of Clinical Failures *(PPDM/CS)* 1612
Marvin C. Meyer, Arthur B. Straughn, Eric J. Jarvi, George C. Wood, Francis R. Pelsor, and Vinod P. Shah

Factors Determining the Intrinsic Lymphatic Partition Rate of Epitiostanol and Mepitiostane *(PPDM)* 1617
Teruhisa Ichihashi, Yasushi Takagishi, and Hideo Yamada

The Effect of Valproate on the Metabolism of Phenobarbital in the Rat *(PPDM)* 1622
Gail D. Anderson and René H. Levy

Influence of Age and Gender on the Plasma Profiles of 3-Hydroxy-3-Methylglutaryl-Coenzyme A (HMG-CoA) Reductase Inhibitory Activity Following Multiple Doses of Lovastatin and Simvastatin *(PPDM/CS)* 1629
Haiyung Cheng, J. Douglas Rogers, Anna E. Sweany, Michael R. Dobrinska, Evan A. Stein, Ann C. Tate, Raju D. Amin, and Hui Quan

Use of Analytically Defined Estimates of Aerosol Respirable Fraction to Predict Lung Deposition Patterns *(APQ/PDD)* 1634
Ted B. Martonen, Ira Katz, Kristen Fults, and Anthony J. Hickey

A High-Performance Liquid Chromatographic Method for the Quantitative Enantioselective Analysis of Mefloquine Stereoisomers *(APQ)* 1640
Yihong Qiu, Satoshi Kitamura, and J. Keith Guillory

Mapping the Ligand Binding Pocket of the Human Muscarinic Cholinergic Receptor Hm1: Contribution of Tyrosine-82 *(MNPC)* 1644
Volkmar Drübbisch, Jelveh Lameh, Mohan Philip, Yogesh K. Sharma, and Wolfgang Sadée

Effects of Diethyl Phthalate and Other Plasticizers on Laurate Hydroxylation in Rat Liver Microsomes *(MNPC/PPDM/Toxicol)* 1648
Richard T. Okita and Janice Rice Okita

Drug Delivery Via Ion Exchange Across a Micromembrane *(PT)* 1654
Dennis R. Jenke, Christopher D. Baron, and Carol L. Mayers

Viscoelastic Properties of Polyacrylic Acid Gels in Mixed Solvents *(PT)* 1659
James S. Chu, Danny M. Yu, Gordon L. Amidon, Norman D. Weiner, and Arthur H. Goldberg

Formulation and Optimization of a Modified Microporous Cellulose Acetate Latex Coating for Osmotic Pumps *(PT)* 1664
Leah E. Appel, James H. Clair, and Gaylen M. Zentner

Chemoprevention of Chemically-Induced Skin Tumor Development by Diallyl Sulfide and Diallyl Disulfide *(Pharmacology)* 1668
Chandradhar Dwivedi, Stacie Rohlfs, Donnita Jarvis, and Ferzaan N. Engineer

TECHNICAL NOTES

Cyclodextrin/Weak-Electrolyte Complexation: Interpretation and Estimation of Association Constants from Phase Solubility Diagrams *(PDD)* 1671
Fang-yu Liu, Dane O. Kildsig, and Ashim K. Mitra

Chemical Stability of Ethyl Icosapentate Against Autoxidation. I. Effect of Temperature on Oxidation Kinetics *(APQ)* 1673
Reiko Teraoka, Makoto Otsuka, and Yoshihisa Matsuda

BOOK REVIEWS

Toxicology of Plant and Fungal Compounds. Handbook of Natural Toxins, Vol. 6 1677
Reviewed by W. T. Shier

Advanced Methods of Pharmacokinetic and Pharmacodynamic Systems Analysis 1677
Reviewed by Bhasker V. Shetty

AUTHOR INDEX TO VOLUME 9 (1992) 1678

SUBJECT INDEX TO VOLUME 9 (1992) 1682